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ON THE NATURE
OF THE
PHOSPHATIC PRECIPITATE
OBTAINED UPON
HEATING URINE.

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NATURE OF THE PHOSPHATIC PRECIPITATE

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HEATING URINE.

The fact that clear urines, free from albumen, and neutral or even faintly acid in reaction,[b] frequently become turbid upon heating is familiar to every one. The turbidity readily and completely disappears upon the addition of a few drops of dilute acid; and this test points to the phosphatic nature of the precipitate, and precludes any possible risk of mistaking it for an albuminous haze, which it closely resembles in appearance. So far as I know, only three explanations of the cause of the turbidity have been put forward:—

1. That the precipitation is occasioned by the heated urine becoming alkaline owing to conversion of some of the urea into ammonium carbonate.

2. That the phosphatic salt is thrown down owing to the expulsion of the free CO_2 from the urine.

3. Scherer ascribed the circumstance to the conversion of the neutral phosphates of calcium and magnesium into basic salts.

In a recent number of the *Zeitschrift für physiologische Chemie*, 1883, VII. Bd., p. 119, among some "Kleinere Mittheilungen" by Professor E. Salkowski of Berlin, is a short article—"Ueber die Löslichkeitsverhältnisse des phosphorsauren Kalkes im Harn"—which attracted my attention. Before making any comments it will be convenient to reproduce Salkowski's observations, so far as necessary, in his own words.

In the first place, Salkowski points out a fact which appears

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[a] Read before the Dublin Biological Club, April 24th, 1883.

[b] Acidity of healthy normal urine is probably due (*a*) to acid phosphate of Na; (*b*) acid urate of Na; and (*c*) ? to free aromatic acids.

to have been hitherto unaccountably overlooked—viz., that urines troubled by heating *frequently become perfectly clear again upon cooling.* This phenomenon—turbidity upon heating and re-solution upon cooling—is exhibited by the 24-hours urine, in the majority of cases, or at least very frequently. When the calcium phosphate is precipitated in a flocculent form—*i.e.*, corresponding to a relatively large separation, the precipitate may not clear up upon cooling.

This precipitation of calcium phosphate is usually attributed to the evolution of the free CO_2 held in solution in the urine. It is undoubtedly true that CO_2 can dissolve calcium phosphate, but whether the urinary CO_2 can play this part is very doubtful, for the amount of this gas in urine (4·4 to 14·3 per cent.) is too small to exercise this solvent action upon calcium phosphate. Again, it is by no means the rule that urine which yields a phosphatic deposit by heat becomes alkaline, or even shows any tendency to alkalescence, in its reaction. This may happen, no doubt, but it is not a condition of the precipitation—on the contrary, no alteration in the reaction is commonly noticed; so that in the majority of cases we cannot admit as causes either the extrication of CO_2 or a partial transformation of urea into ammonium carbonate.

From 100 cc. of acid urine, sp. gr. 1029, heated to boiling, Salkowski obtained a permanent precipitate which weighed 0·0836 grm. The precipitate was free from Mg, and contained an amount of CaO nearly corresponding to the formula $Ca_3P_2O_8$.

The reaction of this urine after the separation of the calcium phosphate underwent no sensible change. The following experiments are adduced by Salkowski in elucidation of the facts described above:—

If a few drops of solution of calcium chloride are added to a solution of primary potassium phosphate (KH_2PO_4), whose strength approximates to the amount in normal urine (*i.e.*, about 0·2 P_2O_8 in 100 cc.), the fluid remains clear. If the liquid be now boiled, calcium phosphate separates out, the reaction remaining acid. But the separation is not complete, for the filtrate from the flocculent gelatinous precipitate still includes phosphoric acid and calcium, and accordingly when warmed with ammonia yields an additional precipitate of calcium phosphate; and lastly, the filtrate from this precipitate still contains alkaline phosphate together with small quantities of chloride of potassium. Thus we can accurately imitate the relations of the urine in a fluid *which contains nothing* *else than phosphoric acid, potassium, calcium, and a small quantity of chlorine.* Solutions of ordinary sodium phosphate (Na_2HPO_4) also furnish the same results when treated with calcium chloride, shaken, and filtered. The filtrate reacts neutral, contains calcium phosphate, although in small amount in solution, and behaves upon heating as described. Freshly precipitated and well-washed calcium phosphate likewise dissolves by agitation in solution of alkaline phosphate—*i.e.*, in (K,Na) H_2PO_4—but only to a slight extent. In these cases and also in urine Salkowski thinks that we evidently have to do with an easily decomposed combination of calcium phosphate and alkaline phosphate. No alteration in the reaction was observed to follow the separation of the calcium phosphate; and, upon theoretical grounds, we would rather expect an *increase* of acidity, since the soluble combinations of phosphoric acid, in which H_2 are replaced by a metal, have an alkaline reaction, but the calcium phosphate, as separated from the urine, contains three atoms of metal, and therefore in the act of precipitation an equivalent of base is withdrawn from the fluid.

Transient cloudiness, which certainly corresponds to a scanty separation, may, perhaps, be regarded as a dissociation phenomenon resulting from elevation of temperature. Whether a urine does or does not deposit calcium phosphate upon heating depends upon two things:—(*a*) upon the reaction; (*b*) upon the proportion of Ca present.

If 100 cc. of a urine which remains clear upon boiling are cautiously treated with dilute solution of calcium chloride, added drop by drop, so as not to cause a precipitate, and the heat test is applied from time to time, we soon arrive at a point when the urine is troubled by heating and clears again upon cooling. Let this point be overstepped, by adding more calcium chloride, and the flocculent precipitate obtained by heat will no longer redissolve upon cooling.

Similar results are obtained by simply neutralising the acid reaction of the urine with one-fourth normal soda solution. But naturally in this case the transient as well as the persistent turbidity is much less, because healthy urine contains very little calcium (0·2–0·4 grm. CaO *per diem.*)

I will now make a few remarks on Salkowski's paper—(*a*) as to the re-solution of the precipitate; (*b*) as to the reaction of the liquid; (*c*) as to the theory of production of the precipitate.

(*a*) In the urines which I have as yet examined I have scarcely succeeded in *entirely* re-dissolving the precipitate by cooling the urine.

(*b*) So far as my observations go, they confirm Salkowski's statement that in urines which become turbid by heat, no decided change in the reaction to test-papers occurs after boiling. In one case I thought the acid reaction was better marked after boiling. I have not met with a urine rendered alkaline by boiling.

(*c*) As to the nature of the precipitate, Salkowski seems to conclude that it corresponds to $Ca_3(PO_4)_2$, and gives one approximate analysis in support of this, but he does not attempt any precise explanation of the facts.

From some experiments made in conjunction with Dr. Emerson Reynolds, to whom I am much indebted, it appears probable that the production of the precipitate depends upon a nice adjustment in the proportions and basicity of the phosphatic salts existing in the urine.

Some pure neutral calcium chloride was prepared, and likewise some pure crystallised acid potassium phosphate (KH_2PO_4). With these two salts alone we failed to imitate the behaviour of the urine, and I am unable to confirm Salkowski's experiment; but on adding a little Na_2HPO_4 to the KH_2PO_4—*i.e.*, reducing the acidity—and then a little calcium chloride, a white, gelatinous, flocculent precipitate was obtained upon boiling, which partially cleared by cooling, the reaction remaining acid.

A similar precipitation and re-solution could be obtained by cautiously treating Na_2HPO_4 with a little phosphoric acid, and then adding calcium chloride. In this way we obtain a mixture of mono- and di-metallic phosphates, and it seems reasonable to conclude that Salkowski may not have operated with a pure salt. It was also found that an excess of acid phosphate re-dissolved completely the precipitate from urine, or the previous addition of a large excess of acid phosphate to the urine prevented precipitation by heat.

Dr. Reynolds was kind enough to prepare for me a solution which exhibits the property in question. Ammonia was very cautiously added to a dilute solution of acid calcium phosphate ($CaH_4P_2O_8$) until a permanent precipitate was just formed; then a few drops more of the acid phosphate were added, and the liquid filtered. Upon boiling the liquid became turbid, and *partially* cleared again upon cooling.

It is known that the acid salt, $Ca_2H_2P_2O_8$ (prepared by action of Na_2HPO_4 on $CaCl_2$), combines with different proportions of water, that it may be crystalline or amorphous and *more or less soluble in acid,* according to the manner of its precipitation, and that it also often contains admixed tribasic phosphate (Ca_32PO_4).—("Watts' Dict. of Chem.," IV., p. 555.)

Either of its hydrates [($Ca_2H_2P_2O_8$, $4H_2O$) or ($Ca_2H_2P_2O_8$, $3H_2O$)] is decomposed by boiling in water. $Ca_2H_2P_2O_8, 3H_2O$ is nearly insoluble in cold water, but its solution is assisted by the presence of NaCl, ammonium salts, organic acids, and CO_2 (conditions some of which exist in urine), and it is resolved by boiling with water into insoluble Ca_32PO_4, and soluble $CaH_4P_2O_8$. Thus $2(Ca_2H_2P_2O_8) = Ca_3P_2O_8 + CaH_4P_2O_8$. Now, we do not know exactly in what state or states calcium phosphates occur in urine, but let us assume that we have in solution at the same time di-calcic and mono-calcic phosphate; then, under suitable conditions of relative proportion and of acidity, we might, as Dr. Reynolds suggests, express the change by heat in this way:—

$$2(Ca_2H_2P_2O_8) + CaH_4P_2O_8 = Ca_3P_2O_8 \text{ (insoluble)} + 2CaH_4P_2O_8 \text{ (soluble)}.$$

Upon reduction of the temperature the inverse change would occur, attended with re-solution of the tricalcic phosphate in part or in full, according to the relative amount of acid phosphates present. So that, in a word, the phenomenon in question seems to be one of unstable equilibrium among certain phosphatic salts,[a] the balance of solubility being easily disturbed by changes of temperature, modified possibly by the kind and amount of other salts in the solution. These considerations tend to throw some light upon the deposition of calcium phosphate within the bladder, and on the formation of urinary calculi, and show how such precipitation may take place in a feebly acid condition of the urine.

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[a] From two-thirds to three-fourths of the PO_4 in urine are combined with K or Na; the rest with Ca and Mg.